Exploring the boundaries of endovascular aneurysm repair

II VALORISATION

An abdominal aortic aneurysm (AAA) is a pathological dilatation and weakening of the abdominal aorta. A dilated aorta can rupture AAA (rAAA), a fatal event if no emergency intervention is performed. To prevent a rupture of an AAA, asymptomatic AAAs require follow-up and need treatment if certain criteria are reached.

In the 1950's the first successful AAA exclusion was performed by open repair, replacing the AAA with a homograft. The homograft was eventually replaced by a synthetic graft. A major drawback of open repair is the need for a laparotomy with cross-clamping of the aorta, a very invasive procedure resulting in substantial risk of complications and death.

In 1991 the first articles of a novel less invasive technique were published.[1,2] Endovascular aneurysm repair (EVAR) is performed by inserting a stent covered with fabric through the femoral arteries and positioning it in the infrarenal aorta. The absence of a laparotomy or cross-clamping the aorta was thought to greatly reduce operative risks and mortality. A reduction of risks also increased the eligibility for elective AAA repair.

Large randomized controlled trials (RCTs) conducted in the late 1990's and early 2000's were designed to compare EVAR to the already proven open repair. These RCTs all showed a significant reduction in both early complications and mortality.[3-5] EVAR was, as a result of the overwhelming data, quickly accepted as the preferred intervention for asymptomatic AAAs. However, under certain circumstances the application of EVAR remained open for discussion. This thesis uses registry data to study the perceived boundaries of conventional EVAR.

Even though the current boundaries for EVAR are generally accepted a lot is still unclear. In **Part one** the use of EVAR in rAAAs is discussed. RCTs have shown no clear advantage of emergency EVAR, yet it is seen by many as the preferred method of treatment for rAAAs.

Part two focuses on the anatomical limitations for conventional EVAR. Manufacturers draft anatomical limitations in their instructions for use (IFU) in which the stent graft is expected to perform well. However, clinical data suggest that these limitations might be too conservative.

For **Part three** long-term outcomes of EVAR were collected. There is controversy how these results should be interpreted. Some physicians are

convinced that, based on these long-term results open repair should be the treatment of choice for AAA repair.[7]

SOCIO-ECONOMIC RELEVANCE

Endovascular treatment of AAAs requires a large amount of resources for both the treatment and post-operative surveillance. Efficient use of stent grafts and customized follow-up schemes might be a way to reduce costs.

Anatomically challenging AAAs might require a custom-made (fenestrated EVAR-) device, that is far more expensive than a conventional (EVAR-) device. The IFU of a stent graft encompasses the anatomical range in which the device is proven to be effective. As mentioned earlier, from clinical experience, devices are expected to be more suitable than defined in the IFU. Increasing the application of conventional EVAR can reduce the need for a more expensive custom-made solution. Although the data presented in this thesis is not sufficient to change an IFU, a registry designed like the EAGLE registry, might.

Complications and the following secondary interventions mandate extensive and lifelong follow-up. Although this is important, studies reporting on historic cohorts are limited. The long-term data of RCTs show an increased need for secondary interventions in the EVAR group. To improve the efficacy of EVAR follow-up, details on anatomy, stent graft selection and indication for intervention are of the utmost importance. In this thesis complications occurring up to 10 years after implantation, but also on the difference between stent grafts, are reported.

Complications occur up to 10 years post implantation but there is a difference between devices. This kind of information can help increase efficacy of follow-up. The variety of stent grafts and indications for a secondary intervention, require large cohort studies in order to be able to identify risk factors. As shown in this thesis differences, with regards to limb patency and proximal sealing, exist and they need to be addressed.

TARGET AUDIENCE

As this thesis presents real-world data, it targets both endovascular specialists and policy makers. Because EVAR has become the preferred treatment for AAAs, research often focuses on novel techniques or

exceptional cases. However, the majority of patients is treated with conventional EVAR using of-the-shelf devices. Information about long-term outcomes and specific device characteristics can assist physicians in determining the best treatment for an individual patient.

Exploring the boundaries of EVAR is part of daily practice for some physicians, sometimes forced by the circumstances or and sometimes accidently. Not only can past experiences avoid future mistakes, it might also help to reduce adjunctive procedures as described in **Chapter 7**.

Even though treatment outside IFU is not part of daily practice for everyone, this thesis shows it is feasible within certain limits and with sufficient experience. In experienced hands an off-the-shelf stent graft can be used in a larger population.

Updating and adjusting guidelines requires reliable and contemporary data. One of the lessons that can be learned from the proposed NICE guidelines is that the endovascular society must be able to support their guidelines with solid data.[7] Registries can become a valuable part of guidelines as they are up-to-date and a reflection of real-world conditions. The acceptance of registries is addressed in the latest European guidelines and supported by the fact that **Chapters 3**, **4** and **5** have become part of the European guidelines.[8]

INNOVATIONS AND THE FUTURE

An RCT is considered the most reliable design to answer scientific questions. Landmark EVAR versus open repair trials are clear about the short-term superiority of EVAR. Long-term outcomes of RCTs show that the short-term benefit is undone by the higher rate of complications in EVAR. However, these data provide a snapshot of the past, not always reflecting current expertise and new materials. Although the results leave no room for interpretation the current relevance of these outcomes can be questioned. Some argue that open repair should be considered as the primary treatment option for AAA, others suggest that new RCTs should be performed to evaluate current practice. Such new trial will be subject to the same criticism as the landmark trials.

For the future, it is important to improve intervention selection and reduce long-term complications. An IFU should never be ignored, but the circumstances might allow to treat patients outside the IFU. Sharing

both success and failure of these cases will increase knowledge of EVAR and possibly prevent others from taking unnecessary risks. Because the percentage of specific complications is low, large study groups are required. Various initiatives are already in action, often promoted by national societies. In the Netherlands the Dutch Surgical Aneurysm Audit (DSAA) is collecting data to get insight in the quality of aneurysm care and to stimulate improvements. The DSAA network could be the basis of a database that also provides follow-up information. However, this requires significant investments and efforts. A lot of data is already present in the patients' files. Intelligent use of hospital systems can improve the storage of data and extraction of that information for a nationwide database. European law is already prepared to facilitate anonymous patient data sharing.

Increased knowledge about stent grafts will result in a more patient specific treatment. This also means that open repair remains a valid treatment option for both elective and emergency AAA procedures.

REFERENCES

1. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg. 1991;5(6):491-9.
2. Volodos NL, Karpovich IP, Troyan VI, Kalashnikova Yu V, Shekhanin VE, Ternyuk NE, et al. Clinical experience of the use of self-fixing synthetic prostheses for remote endoprosthetics of the thoracic and the abdominal aorta and iliac arteries through the femoral artery and as intraoperative endoprosthesis for aorta reconstruction. Vasa Suppl. 1991;33:93-5.
3. Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG, EVAR trial participants. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomised controlled trial. Lancet. 2004;364(9437):843-8.
4. Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. N Engl J Med. 2004;351(16):1607-18.
5. Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT, Jr., Matsumura JS, Kohler TR, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA. 2009;302(14):1535-42.
6. Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. J Vasc Surg. 2011;53(5):1167-73 e1.
7. Abdominal aortic aneurysm: diagnosis and management [press release]. https://www.nice.org.uk/: NICE2018.
8. Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2019 Clinical Practice Guidelines on the Management of Abdominal Aorto-iliac Artery Aneurysms. Eur J Vasc Endovasc Surg. 2019;57(1):8-93.